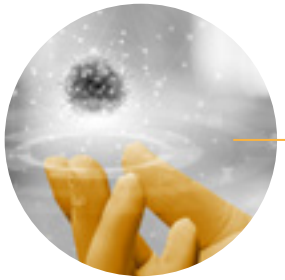

3.3.7 Drug Hypersensitivity and Innate Immune Response Group

Publications: 16
Q1: 6

COMPOSITION

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STRATEGIC OBJECTIVE

Cutaneous adverse drug reactions are unpredictable and represent a plethora of skin diseases with various degrees of severity. The spectrum ranges from mild to potentially fatal multisystem maladies. Those of most concern are usually referred to as severe cutaneous adverse reactions (SCARs), and include acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), also known as drug induced hypersensitivity syndrome or hypersensitivity síndrome (DIHS/HSS), Stevens-Johnson's syndrome (SJS), and toxic epidermal necrolysis (TEN). Among them, SJS and TEN are the most severe clinical entities and are nowadays considered as variants of the same disease characterized by keratinocyte necrosis and epidermal detachment with the formation of subepidermal bullae. From the immunopatohogenic point of view, SCARs are T-cell mediated type IV hypersensitivity reactions. However, T cells can orchestrate different types of immune responses and this functional heterogeneity has led to a further sub-classification into type IVa-IVd hypersensitivity that considers the distinct cytokine production pattern by T cell subpopulations, and emphasizes the participation of different effector cells causing inflammation and tissue damage. Current knowledge supports the active participation of cytotoxic lymphocytes in different clinical entities.

Our project aims to a better understanding of the immune mechanisms underlying the etiopathogenesis of these diseases. The study is performed in the framework of the consortium PIELenRed (Plataforma interdisciplinar para el estudio de reacciones cutáneas graves en red) integrated by researchers belonging to different hospitals in Madrid.

Reactivation of latent herpesvirus has been described during the development of some of the previously mentioned clinical entities. In order to improve our understanding of the behaviour of the immune system during viral replication, collaboration has been established with the Kidney Transplant Unit (Nephrology Service, HULP). Kidney transplant recipients are being followed immediately before and after transplant in order to identify patients with active CMV replication.

General objectives for the next 5 years

The main objectives are:

I) Biobanking of samples of severe cutaneous adverse reactions to medications (DRESS, AGEP and SJS/TEN) associated to the registry PIELenRed, and integrated in the international registry RegiSCAR.

II) To investigate in vitro test for drug causality assessement.
III) To explore the involvement of the innate immune response (in particular natural cytotoxic activity) during the development of SCARs.
IV) Identification of biomarkers of susceptibility.
V) To find biomarkers for disease and response to treatments.
VI) To explore the potential of microRNAs in SJS/TEN as biomarkers of disease and of response to treatments, as well as their relationship with pathogenic mechanisms.
VII) To analyze the evolution of the cytotoxic response in patients with CMV replication.
VIII) Compare the innate immune response in patients with CMV replication after kidney transplant and in patients with SCARs.

RESEARCH LINES

- Biobanking of biological samples from patients with severe cutaneous adverse reactions to medications (DRESS, AGEP and SJS/TEN).
- Development and evaluation of in vtro tests for drug causality assessment.
- Involvement of NK receptors in the etiopathogenesis of Stevens-Johnson syndrome / Toxic epidermal necrolysis (SJS/TEN).
- Identification of biomarkers of susceptibility.
- Differential analysis of the cytokine pattern involved in different SCARs (AGEP, DRESS and SJS/TEN).
- Analysis of miRNAs as biomarkers of disease and response to treatments.
- Identification of biomarkers of response to immunomodulatory treatments.

RESEARCH ACTIVITY

Publications

- Bautista-Villanueva S, Galleani C, Barranco R, Bellón T, Blanco M, García-Moguel I. Acute localized exanthematous pustulosis due to alendronate. J Invest Allerg Clin. 2022; 32(1): 69-70. Editorial Material. IF: 0.604; D1
- Bellón T, González-Valle O, Sendagorta E, Lerma V, del Río JM, Martínez C, Servera G, González-Herrada C, Cachafeiro L, Lorente JA, Cabañas R, Herranz P, de Abajo F. IL-15/IL-15R alpha in SJS/TEN: Relevant expression of IL15 and IL15RA in affected skin. Biomedicines. 2022; 10(8): 1868. Article. IF: 4.7; Q1
- Bellón T, Lerma V, Guijarro J, Ramírez E, Martínez C, Escudero C, Fiandor AM, Barranco R, de Barrio M, de Abajo F, Cabañas R. LTT and HLA testing as diagnostic tools in Spanish vancomycin-induced DRESS cases: A case-control study. Front Pharmacol. 2022; 13: 959321. Article. IF: 5.6; Q1
- Berenguer-Ruiz S, Rivera R, Herranz P, de la Cueva P, Hospital M, Ruiz-Genao D, Roustan G, Dauden E, Llamas-Velasco M. Ustekinumab to guselkumab transitions: A series of 54 patients emulating the navigate trial in real life. Dermatol Ther. 2022; 35(10): e15757. Article. IF: 3.6; Q1
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- Castaño-Fernández JL, Rodríguez-Cuadrado FJ, Sánchez-Gutiérrez I, Najera-Botello L, Fernández IS, Gullón GR, Rosell-Díaz AM. Dermpath & Clinic: Telangiectasia macularis eruptiva perstans. Eur J Dermatol. 2022; 32(4): 556-8. Article. IF: 2.5; Q2
- Elosua-González M, Rosell-Díaz A, Alfageme-Roldán F, Siguenza-Sanz M, Roustán-Gullón G. Clinical remission of disseminated molluscum contagiosum infection in a patient with atopic dermatitis treated with dupilumab. An Bras Dermatol. 2022; 97(3): 358-61. Article. IF: 1.7; Q3
- Fernández IS, Gil MH, Botello LN, Gullón GR. Not all is infantile hemangioma: An erythematous plaque in an adult. Actas Dermosifiliogr. 2022; 113(7): 717-8. Editorial Material. IF: 3.2; Q2
- Fernández-Quiroga C, Alfageme-Roldán F, Roustán-Gullón G. Digital clubbing: Ultrasound findings. Actas Dermosifiliogr. 2022; 113(5): t522-3. Letter. IF: 3.2; Q2
- Laverde-Saad A, Jfri A, García R, Salguero I, Martínez C, Cembrero H, Roustan G, Alfageme F. Discriminative deep learning based benignity/malignancy diagnosis of dermatologic ultrasound skin lesions with pretrained artificial intelligence architecture. Skin Res Technol. 2022; 28(1): 35-9. Article. IF: 2.2; Q3
- Luna-Bastante L, Negrete EL, Naranjo LA, Roustán G, Alfageme F. Sonography of a case series of talar callosities. J Ultrasound. 2022; 25(4): 983-7. Article. IF: 2; Q3
- Páez-Vega A, Gutiérrez-Gutiérrez B, Aguera ML, Facundo C, Redondo-Pachón D, Suner M, López-Oliva MO, Yuste JR, Montejo M, Galeano-Álvarez C, Ruiz-San Millán JC, Los-Arcos I, Hernández D, Fernández-Ruiz M, Muñoz P, Valle-Arroyo J, Cano A, Rodríguez-Benot A, Crespo M, Rodelo-Haad C, Lobo-Acosta MA, Garrido-Gracia JC, Vidal E, Guirado L, Cantisán S, Torre-Cisneros J. Immunoguided discontinuation of prophylaxis for cytomegalovirus disease in kidney transplant recipients treated with antithymocyte globulin: A randomized clinical trial. Clin Infect Dis. 2022; 74(5): 757-65. Article. IF: 11.8; D1
- Pérez AMG, Botello LN, Massa DS, Gullón GR, Roldán FA. Sonography of subcutaneous nodules following immunization with histopathological correlation: a three-case series. J Ultrasound. 2022; 25(2): 355-60. Article. IF: 2; Q3
- Rodríguez-Sanz A, Sánchez-Villanueva R, Domínguez-Ortega J, Álvarez L, Fiandor A, Nozal P, Sanz P, Pizarro-Sánchez MS, Andrés E, Cabezas A, Pérez-Alba A, Bajo MA, Selgas R, Bellón T. Characterization of hypersensitivity reactions to polysulfone hemodialysis membranes. Ann Allerg Asthma Im. 2022; 128(6): 713-20. Article. IF: 5.9; Q2
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Research projects

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Managment centre: FIBHULP

Bellón Heredia T. Impacto de los inhibidores de calcineurina sobre linfocitos efectores citotóxicos en síndrome de Stevens-Johnson/ necrolisis epidérmica tóxica de análisis de il-15 como biomarcador (PI18/00718). ISCIII. 2019-2023.

Managment centre: FIBHULP

Bellón Heredia T. Creación de un centro de referencia para el estudio de los mecanismos implicados en las reacciones de hipersensibilidad a las membranas de hemodiálisis basadas en polysulfona (PI-3009). Nipro Euope NV. 2017-Ongoing.

Managment centre: FIBHULP

de **las Vecillas Sánchez L.** Estudio de la inmunomodulación celular inducida en las desensibilizaciones a quimioterápicos tras reacciones inmediatas y tardías. Sociedad Española de Alergología e Inmunología Clínica (SEAIC). 2022-2024.

Managment centre: Fundación SEAIC

Bellón Heredia T. ELISpot como método diagnóstico para identificación del fármaco causal en pacientes con reacciones graves de hipersensibilidad cutánea a medicamentos: comparación con TTL" (Beca Luis Álvarez). FIBHULP. 2022-2023.

Managment centre: FIBHULPi

Patents and trademarks

Selgas Gutiérrez R, Bellón Heredia T, Rodríguez Sanz AI, Álvarez Builla J, Vaquero López JJ, Sánchez Alonso P, Alajarín Fernández R, inventors; FIBHULP, Universidad de Alcalá, assignees. Use of compounds derived from salts of pyridazine[1',6':1,2]pyrido[3,4-b]indolinium as anti-inflammatory agents. P201331143, PCT/ES2014/070603; 2013 July 25.

Selgas Gutiérrez R, Bellón Heredia T, Rodríguez Sanz AI, Álvarez Builla J, Vaquero López JJ, Sánchez Alonso P, Alajarín Fernández R, inventors; FIBHULP, Universidad de Alcalá, assignees. Use of compounds derived from salts of piridazine[3,2-b]benzimidazolium as anti-inflammatory agents. P201430411, PCT/ES2014/070603; 2013 July 25.